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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/955,216 | 09/19/2001 | Sherri M. Brown | 16517.257 | 1690 |

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| EXAMINER | |
|---|---|
| SITTON, JEHANNE SOUAYA | |
| **ART UNIT** | **PAPER NUMBER** |
| 1634 | |

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/955,216 | BROWN ET AL. | |
| | Examiner | Art Unit | |
| | Jehanne S Sitton | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on 11/5/04

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 10,20,21,24 and 25 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 10,20,21,24 and 25 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. In view of the appeal brief filed on 11/5/2004, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

2. The examiner reviewing your application at the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to examiner Jehanne Sitton.

3. Claims 10, 20, 21, 24, and 25 are pending and under examination. The following rejections contain new grounds of rejection and represent the complete set being presently applied to the instantly pending claims. Responses to the appeal brief follow, where appropriate. Response to arguments made in any previous office action are maintained with regard to the instantly pending claims, as they apply to the rejections and claim interpretations set forth below. The rejection of claims 10, 24-25 under 35 USC 112, first paragraph with regard to Written Description, and the rejection of claims 24-25 under 35 USC 112/second paragraph are withdrawn. The following office action is NON-FINAL.

## *New Grounds of Rejection*

### *Claim Rejections - 35 USC § 101*

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 10, 20-21, and 24-25 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The claims are drawn to an isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 7 (claims 10 and 21). Claims 20 and 21 are drawn to nucleic acids that encode a copalyl diphosphate synthase enzyme (hereinafter referred to as CPS) or a fragment thereof, wherein the nucleic acid hybridizes to SEQ ID NO: 7 or the complement of SEQ ID NO: 7, (claim 21 further stipulates that the nucleic acid which hybridizes to SEQ ID NO: 7 or it's complement comprises SEQ ID NO: 7 or it's complement). Claims 24 and 25 are drawn to nucleic acid molecules that comprise a nucleic acid that shares between 98-100% identity with SEQ ID NO: 7 or it's complement. Claims 10 and 21 do not allow for internal variations within SEQ ID NO: 7 or it's complement, and encompass genes, full open reading frames, fusion constructs and cDNAs. Claims 24, and 25, do allow for internal variations, as does claim 20 by the recitation of hybridization conditions because sequences need not be completely complementary to hybridize to another sequence. Such claims further encompass mutants, variants, and homologs from any plant, of these genes, full open reading frames, fusion constructs and cDNAs (see for example pages 41-42 of the specification which asserts that the

enzymes or fragments of gibberellin pathway enzymes of the present invention are homologues of other plant gibberellin pathway enzymes).

The specification teaches that SEQ ID NO: 7 was identified from library CMz031 (Lib148) (Table A and p. 170). The specification teaches that the library-designated CMz031 was cDNA prepared from maize pollen tissue at a particular developmental stage (V10+, p. 170). The specification asserts that SEQ ID NO: 7 encodes a maize or soybean copalyl diphosphate synthase enzyme [and would presumably be used in the gibberellin pathway to obtain gibberellin], or a fragment thereof (p. 16, lines 15-17) and is therefore useful to identify and obtain homologues in both maize and non-maize plants (see pages 42-43, line 20 to line 4 respectively).

The utilities for the claimed nucleic acids stem from their potential ability, a) to encode copalyl diphosphate synthase, and b) to be used as a probe, that is to hybridize to other nucleic acids to obtain the full length sequence of SEQ ID NO: 7, homologues, or to determine expression (see specification page 73).

The specification provides no evidence that SEQ ID NO: 7 encodes a CPS, or that it was successfully used as a probe to obtain a functional CPS in plants (either a full length cDNA comprising SEQ ID NO: 7 and encoding a functional CPS or functional homologues in maize and non-maize plants) or to determine mRNA expression.

The utilities are based upon homology/identity to experimentally known sequences of the cDNA for maize kaurene synthase A, also known as copalyl diphosphate synthase (g1576885, 03-Aug-1995; Table A and p. 42). CPS catalyzes the first committed step in diterpenoid biosynthesis leading to gibberellins in plants. It cyclizes gerenylgeranyl

diphosphate (GGD) to copalyl diphosphate (CP). A sequence alignment revealed that nucleotides 60-470 of SEQ ID NO: 7 (SEQ ID NO: 7 is 470 nucleotides long) possessed 93.4% identity to nucleotides 2104-2512 of Zea mays kaurene synthase A (an1).

The asserted utilities are neither specific nor substantial because the disclosed uses (ie, use as a hybridization probe) are generally applicable to broad classes of this subject matter. In addition, further characterization of the claimed subject matter (for example, use to encode a peptide with catalytic function – see specification page 37, end of 4th full para) would be required to reasonably confirm a "real world" use, as evidenced by the teachings of the art as set forth below.

Firstly, it is known that for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed nucleotide and the indicated similar nucleotides of known function and therefore lacks support regarding utility. Several publications document the unpredictability of the relationship between sequence and function. For example, Van de Loo et al (PNAS, vol. 92, pages 6743-6747 (1995) teaches that polypeptides of approximately 67% homology to a desaturases in Arabidopsis were found to be a hydroxylases once tested for activity. Seffernick et al (J. Bacteriol. Vol 183, pages 2405-2410; 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid identity catalyze two different reactions, deamination and dehalogenation. Broun et al (Science, vol. 282, pages 1315-1317, 1998) teaches that as few as

four amino acid substitutions can convert an oleate 12 desaturase into a hydroxylase and as few as six amino acid substitutions can transform a hydroxylase into a desaturase. See also, [(Gerhold et al. BioEssays, vol. 18, n. 12, pp. 973-9814; 1996), (Wells et al. J. Leukocyte Biol., vol. 61, n. 5, pp. 545-550; 1997); and (Russell et al. J Molecular Biol., vol. 244, pp. 332-350; 1994)].

The art provides further reason to doubt whether SEQ ID NO: 7 itself or whether the full cDNA (if one exists) that comprises SEQ ID NO: 7 will successfully encode a functional enzyme. From the sequence alignment with An1, it appears that SEQ ID NO: 7 is only a partial fragment of a putative full length cDNA. The 93.4% similarity exists with the portion of the nucleic acid which encodes the extreme C terminal end of An1. The art, however, teaches that such a fragment of An1 would not be expected to have copalyl diphosphate synthase activity. Smith et al (Plant Physiol. 1998, pages 1411-1419) teaches an alignment of plant CPS's including An1 (see Figure 1), and teaches that truncation mutants revealed that once the enzyme was truncated up to a certain point on the N-terminus in pumpkin CmCPS1 and CmCPS2, that such enzymes lacked activity (see figure 1, inverted triangle and legend). If SEQ ID NO: 7 encodes a fragment of a functional CPS, it is no where near this N terminal point. Further, the art provides reason to doubt whether a full length cDNA that comprises SEQ ID NO: 7 even exists, and if so, if it would encode a functional CPS or a pseudogene. Sakamoto et al (Plant Physiol. Vol. 134, pages 1642-1653, 2004) teaches that in rice, a number of CPS-like sequences were found, including one which turned out to be a non functional pseudogene (see table 1, OsCPS3). Sakamoto teaches that other homologues might have different functions than those for OsCPS1 and An1 (see page 1644, col. 2, last sentence of first full para). Sakamoto also teaches

of the frequent presence of small pieces of CPS-like sequences in the rice genome (see page 1652, col. 1, last sentence of para 2). While the specification asserts that the nucleic acids of the specification encode a gibberellin pathway enzyme or "fragment thereof", it is unclear what use the "fragment" that SEQ ID NO: 7 appears to be, would have in any catalytic or enzymatic capacity given the teachings of the pre and post filing date art as noted above. The specification provides no evidence of any catalytic or enzymatic activity for a peptide encoded by SEQ ID NO: 7.

As previously noted, the specification also asserts that SEQ ID NO: 7 can be used to hybridize to another nucleic acid molecule (page 37, 4th full para; page 38-page 39), that sequences with less than 100% identity to SEQ ID NO: 7 could be used to hybridize to SEQ ID NO: 7 or it's complement (last para of page 39-page 41), to obtain homologues (page 43), and to be used as markers (pages 46-49).

The specification has provided no evidence of any successful use of SEQ ID NO: 7 for any of these purposes. As already noted, further experimentation would be required to reasonably confirm that SEQ ID NO: 7 would encode a peptide with any catalytic or enzymatic activity. The specification provides no evidence that the expression of SEQ ID NO: 7 is associated with any particular phenotype or trait, such that no specific or substantial use for SEQ ID NO: 7 as a marker, or to determine mRNA expression, is apparent. Given the state of the post filing date art, it is reasonable to assume that more than one CPS exists in maize. Through mutational analysis, An1 has been shown to be a functional CPS in maize (see Bensen et al, The Plant Cell, vol. 7, pages 75-84, 1995). A homozygous deletion mutant of An1 accumulated ent-kaurene to 20% of wild type levels, indicating the presence of isoenzymes (see page 436 of

Hedden & Kamiya, Ann. Rev. Plant Physio. Plant Mol. Biol. 1997, pages 431-460, 1997). A second putative CPS homologue has been isolated in maize (termed An2), however, to date, it's function or activity have not been confirmed. Sequence analysis has revealed that it does not comprise SEQ ID NO: 7. Therefore, it appears that maize could contain a number of putative CPS-like sequences (see specification Table A, page 210). However, as evidenced by the post filing date art of Sakamoto, there is reason to doubt whether all of these sequences are associated with a full length nucleic acid which encodes a functional enzyme. Sakamoto teaches that one possible explanation for the presence of CPS like sequences which do not function in gibberellin biosynthesis is that multiple copies are deleterious for growth and development, as discussed by Aubourg with regard to Arabidopsis (see page 1652, end of col. 1). Sakamoto acknowledges the need for further experimentation in the form of biochemical studies to confirm such. In the instant case, further experimentation would be required to confirm a "real world" use for SEQ ID NO: 7, either as a marker (that is, the specification provides no evidence that it is a marker for anything), or as a nucleic acid itself to be detected (the specification has provided no evidence that the detection of SEQ ID NO: 7 itself provides any specific, substantial or real world use).

The possible use of SEQ ID NO: 7 as a probe to isolate or detect homologues in maize and non maize plants is dependent on the hybridization conditions used for the analysis. Depending on the conditions of stringency of hybridization and wash, for example a lowering of stringency, there would be a greater likelihood that a large number of different nucleic acids would be detected (that is, nucleic acids encoding different proteins with different functions). There would be no reasonable expectation that all nucleic acids detected would have the same function, (or as evidenced by the teachings of the art: that the sequences would have any

function), or what that function would be. Further experimentation would be required to reasonably confirm the "real world" use for detection or isolation of these nucleic acids. In such case, the use of SEQ ID NO: 7 would be like that of any uncharacterized EST with no specific, substantial or real world use. In response to a rejection (see Office action mailed 5/5/2004, page 19) asserting hybridization of the nucleic acid encoding An1 (sequence taught by Genbank Accession number L37750), which possesses 384 matches to SEQ ID NO: 7 and has 93.4 % identity, and could be considered a "homologue", the appeal brief mailed 11/5/ 2004 asserts that no evidence is present to suggest that SEQ ID NO: 7 would hybridize to L37750 (see appeal brief, page 30, section (b)). Such response raises the question that if SEQ ID NO: 7 does not hybridize to the nucleic sequence of L37750, which it possesses the highest homology to, of any known sequence, under the low stringency conditions set forth in claim 20, than which other homologues would it hybridize to, and therefore what specific, substantial, or well established use would it have as a probe? If it can't be reasonably expected to hybridize to a sequence with the indicated structural nucleic acid similarity (though it should be noted that a certain degree of structural similarity or identity does not predictably correlate to the same or similar function of encoded protein as already discussed above) even under conditions of low stringency (conditions in claim 20, as evidenced by the specification), then further experimentation would be required to reasonably confirm the use of SEQ ID NO: 7 as a probe to isolate or detect expression of CPS's in maize and non maize plants.

However, as noted in Brenner v. Manson, 383 U.S. 519, 535-536 (1996), "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing... a patent is not a hunting license. It is not a reward for

the search, but compensation for its successful conclusion". The specification provides no evidence that SEQ ID NO: 7 encodes a CPS, or that it was successfully used as a probe to obtain a functional CPS in plants (either a full length cDNA comprising SEQ ID NO: 7 and encoding a functional CPS or functional homologues in maize and non-maize plants) or to determine mRNA expression or that any polymorphisms exist, and if so, what they would be used for.

***Response to Arguments***

The appeal brief mailed 11/5/2004 traverses the rejection. All arguments have been thoroughly reviewed but were not persuasive for the reasons which follow. Any arguments with regard to SEQ ID NO: 7 encoding a maize copalyl diphosphate synthase enzyme (page 6, 2nd and 3rd full para, pages 9-11) are not found persuasive as the art provides strong evidence to suggest that the peptide encoded by SEQ ID NO: 7 would have no enzymatic activity. While the specification generally asserts that the nucleic acids of the invention encode enzymes of the gibberellin biosynthetic pathway in maize or soybean, the specification provide no evidence that any of the nucleic acids, nor specifically SEQ ID NO: 7, encode proteins with enzymatic activity. With regard to encoding a fragment of a CPS, again, SEQ ID NO: 7 appears to encode a fragment that would have no CPS activity (see Smith et al; Figure 1, legend, discussion of conserved sequence motifs and N terminal truncation studies). An alignment with An1, a maize CPS, shows that SEQ ID NO: 7 does not possess or encode any of these sequences necessary for activity as a CPS. Therefore, the use of SEQ ID NO: 7 to encode a maize CPS is not a substantial utility. Further experimentation would be required to reasonably confirm that a peptide encoded by SEQ ID NO: 7 would have CPS activity.

At page 7-8, the brief traverses that the lack of utility analysis misstates the asserted uses, ignores disclosed utilities, and misapplies the doctrine of "practical utility" and applies case law in support for the doctrine of "practical utility" and the requirement for "identifiable benefit". These arguments are not specifically drawn to the rejection set forth previously or above, and are an allegation. They are found non-persuasive and are reasonably an introductory summary set forth by the brief. As a preliminary matter, the rejections in this application are made in order to comply with office policy regarding the utility guidelines (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for Utility.). So to the extent that any argument conflicts with the guidelines, it will necessarily be non-persuasive.

At pages 11-12, the appeal brief discusses identifying the presence or absence of a polymorphism. All discussion of polymorphisms in the specification is generic in nature, suggesting that the polymorphisms and microsattelites to be identified may exist, but none are identified. The specification lacks a discussion of any specific or substantial phenotypic association or even predisposition regarding any claimed nucleic acid. This lack of such association can only be remedied, if such an association with any phenotype even exists for the instantly claimed nucleic acids, by further research. It is also unknown what such research may or may not find regarding the instantly claimed nucleic acid molecules. This supports the lack of a currently available utility for the instantly claimed invention as is the basis for the lack of utility rejection against the instant claims. The identification of the presence of absence of a polymorphism is strictly speaking a hunting license which requires further research to obtain the presence of a polymorphism. Furthermore, even if the polymorphism is determined, the presence or absence of a polymorphism does not have a clear utility. Polymorphisms are natural

variations within sequences which themselves may not have any meaningful use. Therefore, determining whether the claimed nucleic acids have or do not have a polymorphism would require determining whether there was a polymorphism within such a sequence and then determining how to use this information in a patentably meaningful way. The appeal brief also traverses, "many of these uses are directly analogous to a microscope". This argument has been reviewed but is not persuasive because the microscope provides information to the scientist which is automatically useful. For example, the microscope may be used for identification and differentiation between gram-positive and gram-negative bacteria. The differentiation of bacteria facilitates in the administration of proper antibiotics. For example, if the microscope is used to determine whether Staph is present or whether Strep is present provides valuable information to the scientist and/or doctor for treating patients. A gas chromatograph is well known to be useful for detection of toxic material, for example. These uses are well known and beneficial in that results are already determined which are useful for at least one analysis type. The instant invention, however, provides no information to this extent. If the scientist determines that a polymorphism in SEQ ID NO: 7 is present, the scientist does not know how to use this information. Such use, is therefore not considered a substantial utility.

The appeal brief at pages 12-15 traverses that the claimed nucleic acids can be used as probes or a source for primers and specifically asserts that the claimed nucleic acids could be used to isolate the promoter association with the nucleic acid. A discussion of use of SEQ ID NO: 7 with regard to hybridization (probes and primers) is set forth in the rejection above. Also, as set forth above, there is no evidence set forth in the specification that a full length gene comprising SEQ ID NO: 7 exists, whereas the art provides evidence that plants can contain

multiple CPS like sequences that are either CPS like fragments, or pseudogenes. As such, it is not known whether or not a promoter for SEQ ID NO: 7 exists. With regard to the use for the claimed nucleic acid with regard to providing a useful starting point for a chromosomal walk such argument thoroughly reviewed but not found persuasive because the specification fails to demonstrate that any of the claimed nucleic acid molecules would be useful in obtaining successful result from such search.

The traversal at page 16, first full para, of the appeal brief regarding polymorphisms and encoding a peptide with CPS activity have been addressed. At pages 16-17, the appeal brief traverses that there is no question that the public has recognized the benefits provided by the claimed subject matter, however, it provides no arguments with regard the claimed subject matter, only a general commentary about EST molecules. This is not persuasive because it does not overcome the fact that the specification does not provide any utility that does not require further experimentation to reasonably confirm that it is in fact applicable in a specific manner to the instantly claimed subject matter. The appeal brief traverses that a multi-million dollar industry has been established for ESTs which may also find utility as industrial products for fermentation processes. In response, there is no instant support for the instantly claimed nucleic acid molecules being of monetary value. The brief at page 17 traverses that the market participants for EST products are primarily sophisticated corporations with highly knowledgeable scientists. This argument has been thoroughly reviewed but was not found persuasive as no market value has been determined or even alleged for the instantly claimed nucleic acids.

With regard to arguments concerning credibility, the credibility of the asserted uses has not been challenged. It is acknowledged that polymorphism analysis, for example, are credible utilities, but that a lack of utility still exists if there is no well established utility or either a specific or substantial utility as is the situation for the instantly claimed invention.

### *Claim Rejections - 35 USC § 112*

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10, 20, 21, 24, and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making the nucleic acid sequence of SEQ ID NO: 7 or it's complement, does not reasonably provide enablement for making or using the nucleic acids encompassed by the broad scope of claims 10, 20, 21, 24, and 25. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Additionally, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above in section 5, one skilled in the art clearly would not know how to use the claimed invention.

There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue. These factors have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are drawn to an isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 7 (claims 10 and 21). Claims 20 and 21 are drawn to nucleic acids that encode a copalyl diphosphate synthase enzyme (hereinafter referred to as CPS) or a fragment thereof, wherein the nucleic acid hybridizes to SEQ ID NO: 7 or the complement of SEQ ID NO: 7, (claim 21 further stipulates that the nucleic acid which hybridizes to SEQ ID NO: 7 or it's complement comprises SEQ ID NO: 7 or it's complement). Claims 24 and 25 are drawn to nucleic acid molecules that comprise a nucleic acid that shares between 98-100% identity with SEQ ID NO: 7 or it's complement. Claims 10 and 21 do not allow for internal variations within SEQ ID NO: 7 or it's complement, and encompass genes, full open reading frames, fusion constructs and cDNAs. Claims 24, and 25, do allow for internal variations, as does claim 20 by the recitation of hybridization conditions because sequences need not be completely complementary to hybridize to another sequence. Such claims further encompass mutants, variants, and homologs from any plant, of these genes, full open reading frames, fusion constructs and cDNAs (see for example pages 41-42 of the specification which asserts that the enzymes or fragments of gibberellin pathway enzymes of the present invention are homologues of other plant gibberellin pathway enzymes). However, the specification provides insufficient guidance for the skilled artisan to make or use the broad scope of nucleic acids encompassed by the instantly pending claims.

The specification teaches that SEQ ID NO: 7 was identified from library CMz031 (Lib148) (Table A and p. 170). The specification teaches that the library-designated CMz031 was cDNA prepared from maize pollen tissue at a particular developmental stage (V10+, p. 170). The specification asserts that SEQ ID NO: 7 encodes a maize or soybean copalyl diphosphate synthase enzyme [and would presumably be used in the gibberellin pathway to obtain gibberellin], or fragment thereof (p. 16, lines 15-17) and is therefore useful to identify and obtain homologues in both maize and non-maize plants (see pages 42-43, line 20 to line 4 respectively). The uses set forth by the specification for SEQ ID NO: 7 are based upon homology/identity to experimentally known sequences of the cDNA for maize kaurene synthase A, also known as copalyl diphosphate synthase (g1576885, 03-Aug-1995; Table A and p. 42). CPS catalyzes the first committed step in diterpenoid biosynthesis leading to gibberellins in plants. It cyclizes gerenylgeranyl diphosphate (GGD) to copalyl diphosphate (CP). A sequence alignment revealed that nucleotides 60-470 of SEQ ID NO: 7 (SEQ ID NO: 7 is 470 nucleotides long) possessed 93.4% identity to nucleotides 2104-2512 of Zea mays kaurene synthase A (an1). However, the specification provides no evidence that SEQ ID NO: 7 encodes a CPS, or that it was successfully used as a probe a) to obtain a functional CPS in plants (either a full length cDNA comprising SEQ ID NO: 7 and encoding a functional CPS or functional homologues in maize and non-maize plants), or b) to determine mRNA expression, or c) that it can be used as a marker.

Given the state of the art and the unpredictability of the art as set forth below, it would require undue experimentation for the skilled artisan to make or use the broad scope of nucleic acids encompassed by the claims.

Due to the term "comprising", all of the claims encompass the full length gene and cDNA sequences that comprise SEQ ID NO: 7 or its complement. Claims 20 and 21 specifically encompass sequences that encode a peptide with copalyl diphosphate synthase activity. However, the art provides reason to doubt that SEQ ID NO: 7 itself will successfully encode a functional enzyme with copalyl diphosphate synthase activity. From the sequence alignment with An1, it appears that SEQ ID NO: 7 is only a partial fragment of a putative full length cDNA. The 93.4% similarity exists with the portion of the nucleic acid which encodes the extreme C terminal end of An1. The art, however, teaches that such a fragment of An1 would not be expected to have copalyl diphosphate synthase activity. Smith et al (Plant Physiol. 1998, pages 1411-1419) teaches an alignment of plant CPS's including An1 (see Figure 1), and teaches that truncation mutants revealed that once the enzyme was truncated up to a certain point on the N-terminus in pumpkin CmCPS1 and CmCPS2, that such enzymes lacked activity (see figure 1, inverted triangle and legend). If SEQ ID NO: 7 encodes a fragment of a functional CPS, it is no where near this N terminal point. Further, the art provides reason to doubt whether a full length cDNA or gene that comprises SEQ ID NO: 7 even exists, and if so, if it would encode a functional CPS or a pseudogene. Sakamoto et al (Plant Physiol. Vol. 134, pages 1642-1653, 2004) teaches that in rice, a number of CPS-like sequences were found, including one which turned out to be a non functional pseudogene (see table 1, OsCPS3). Sakamoto teaches that other homologues might have different functions than those for OsCPS1 and An1 (see page 1644, col. 2, last sentence of first full para). Sakamoto also teaches of the frequent presence of small pieces of CPS-like sequences in the rice genome (see page 1652, col. 1, last sentence of para 2). Therefore, given the teachings of the art, it would require undue experimentation to

make the nucleic acids encompassed by the claims. While the specification generally teaches how to use nucleic acid sequences as hybridization probes, and while SEQ ID NO: 7 (or its complement) could be used to isolate a full length sequence which comprises SEQ ID NO: 7 (or its complement), there is reason to doubt whether such a full length sequence exists. The teachings of the specification provide one of skill in the art with a teaching of how to find nucleic acids that would fall within the scope of the claims. Such is not a teaching of the combination of nucleotide bases that would encode a copalyl diphosphate synthase enzyme comprising SEQ ID NO: 7. Therefore, given the lack of guidance from the specification and the unpredictability of the art, undue experimentation would be required for the skilled artisan to make a full length gene or cDNA sequence comprising SEQ ID NO: 7 which encoded copalyl diphosphate synthase.

Additionally, claims 20, 24, and 25 encompass homologues and claims 24 and 25 further encompass mutants of SEQ ID NO: 7 and sequences comprising SEQ ID NO: 7, that is full length gene or cDNA. However, it is known that for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed nucleotide and the indicated similar nucleotides of known function and therefore lacks support regarding enablement. Several publications document the unpredictability of the relationship between sequence and function. For example, Van de Loo et al (PNAS, vol. 92, pages 6743-6747 (1995) teaches that polypeptides of approximately 67%

homology to a desaturases in Arabidopsis were found to be hydroxylases once tested for activity. Seffernick et al (J. Bacteriol. Vol 183, pages 2405-2410; 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid identity catalyze two different reactions, deamination and dehalogenation. Broun et al (Science, vol. 282, pages 1315-1317, 1998) teaches that as few as four amino acid substitutions can convert an oleate 12 desaturase into a hydroxylase and as few as six amino acid substitutions can transform a hydroxylase into a desaturase. See also, [(Gerhold et al. BioEssays, vol. 18, n. 12, pp. 973-9814; 1996), (Wells et al. J. Leukocyte Biol., vol. 61, n. 5, pp. 545-550; 1997); and (Russell et al. J Molecular Biol., vol. 244, pp. 332-350; 1994)]. The specification fails to teach which specific nucleotides can be altered by the skilled artisan without altering the function of the putative CPS encoded by SEQ ID NO: 7. Each variation results in a new and independent sequence that does not reliably result in similar or identical activity of the encoded peptide, as evidenced by the teachings of the art. Therefore, given the lack of guidance from the specification and the unpredictability of the art, undue experimentation would be required for the skilled artisan to make homologues and mutants of SEQ ID NO: 7 or sequences comprising SEQ ID NO: 7, as is encompassed by the claims.

With regard to use of SEQ ID NO: 7 and homologues of SEQ ID NO: 7 (encompassed by claims 20, 24, and 25), as noted above, SEQ ID NO: 7 appears to be a partial fragment of a putative CPS. This fragment does not appear to encode a peptide with any copalyl diphosphate synthase activity. The potential use for SEQ ID NO: 7 is not limited to its ability to encode a peptide, however. The specification also asserts that SEQ ID NO: 7 can be used to hybridize to another nucleic acid molecule (page 37, 4$^{th}$ full para; page 38-page 39), that sequences with less

than 100% identity to SEQ ID NO: 7 could be used to hybridize to SEQ ID NO: 7 or it's complement (last para of page 39-page 41), to obtain homologues (page 43), and to be used as markers (pages 46-49). However, the specification has provided no evidence of any successful use of SEQ ID NO: 7 for any of these purposes. The specification provides no evidence that the expression of SEQ ID NO: 7 is associated with any particular phenotype or trait, such that no use for SEQ ID NO: 7 as a marker, or to determine mRNA expression, is apparent. Accordingly, even if SEQ ID NO: 7 were to contain a polymorphism, the skilled artisan would not be able to use the polymorphism information in any way other than to determine what effect it might have on a plant phenotype transformed with the nucleic acid of SEQ ID NO: 7. Given the state of the post filing date art, it is reasonable to assume that more than one CPS exists in maize. Through mutational analysis, An1 has been shown to be a functional CPS in maize (see Bensen et al, vol. 7, pages 75-84, 1995). A homozygous deletion mutant of An1 accumulated ent-kaurene to 20% of wild type levels, indicating the presence of isoenzymes (see page 436 of Hedden & Kamiya, Ann. Rev. Plant Physio. Plant Mol. Biol. 1997, pages 431-460, 1997). A second putative CPS homologue has been isolated in maize (termed An2), however, to date, its function or activity have not been confirmed. Sequence analysis has revealed that it does not comprise SEQ ID NO: 7. Therefore, it appears that maize could contain a number of putative CPS-like sequences (see specification Table A, page 210). However, as evidenced by the post filing date art of Sakamoto, there is reason to doubt whether all of these sequences are associated with a full length nucleic acid which encodes a functional enzyme. Sakamoto teaches that one possible explanation for the presence of CPS like sequences which do not function in gibberellin biosynthesis is that multiple copies are deleterious for growth and development, as discussed by Aubourg with regard to

Arabidopsis (see page 1652, end of col. 1). Sakamoto acknowledges the need for further experimentation in the form of biochemical studies to confirm such. In the instant case, further unpredictable experimentation would be required to determine how to use SEQ ID NO: 7 as a marker (that is, the specification provides no evidence that it is a marker for anything). The possible use of SEQ ID NO: 7 as a probe to isolate or detect homologues in maize and non maize plants is dependent on the hybridization conditions used for the analysis. Depending on the conditions of stringency of hybridization and wash, for example a lowering of stringency, there would be a greater likelihood that a large number of different nucleic acids would be detected (that is, nucleic acids encoding different proteins with different functions). There would be no reasonable expectation that all nucleic acids detected would have the same function, (or as evidenced by the teachings of the art: that the sequences would have any function), or what that function would be. Given that the ability of two sequences to hybridize to each other is based on their nucleic acid structure, which does not necessarily correlate to any predictably similar function for the peptides encoded by such nucleic acids, further experimentation would be required to determine a use for the nucleic acids that would hybridize to SEQ ID NO: 7 or homologues of SEQ ID NO: 7 (as encompassed by claims 20, 24, and 25). In response to a rejection (see Office action mailed 5/5/2004, page 19) asserting hybridization of the nucleic acid encoding An1 (sequence taught by Genbank Accession number L37750), which possesses 384 matches to SEQ ID NO: 7 and has 93.4 % identity, and could be considered a "homologue", the appeal brief mailed 11/5/ 2004 asserts that no evidence is present to suggest that SEQ ID NO: 7 would hybridize to L37750 (see appeal brief, page 30, section (b)). Such response raises the question that if SEQ ID NO: 7 does not hybridize to the nucleic sequence of L37750, which it

possesses the highest homology to, of any known sequence, under the low stringency conditions set forth in claim 20, than which other homologues would it hybridize to, and therefore what use would it have as a probe? If it can't be reasonably expected to hybridize to a sequence with the indicated structural nucleic acid similarity even under conditions of low stringency (conditions in claim 20, as evidenced by the specification), then further unpredictable trial and error experimentation would be required to reasonably confirm the use of SEQ ID NO: 7 as a probe to isolate or detect expression of CPS's in maize and non maize plants.

***Response to Arguments***

The appeal brief at page 19 traverses that the "make and test" quantum of experimentation is reduced by extensive knowledge. In the instant case, the art provides strong evidence to suggest that SEQ ID NO: 7 does not encode a peptide with CPS activity, and provides reasons to doubt that a full length gene or cDNA comprising SEQ ID NO: 7 exists. Such issues have been addresses in the rejection set forth above, which are newly applied. The use for the claimed nucleic acids to isolate other sequences within the genome has also been addressed above (with regard to arguments at the beginning of page 20 of the brief), as have the use of hybridization conditions. With regard to the 4$^{th}$, 5$^{th}$, and 6$^{th}$ Wands factors (page 20 of brief, first full para), the specification has provided general teachings of hybridization analysis to isolate or detect other nucleic acid sequences. However, such represent teachings of how to find embodiments that are encompassed by the broad scope of the claimed nucleic acids. In the instant case, there is no evidence that expression of SEQ ID NO: 7 in a cell or plant would have any phenotypic effect. With regard to the predictability in the art, the rejection above sets forth the unpredictability in the art with regard to making or using nucleic acid encompassed by the

broad scope of the claimed invention. Any arguments regarding lack of evidence are found non persuasive in view of the evidence in the form of scientific articles analyzing the state of the art and the unpredictability of the art, newly applied and set forth in the rejection above.

7. Claims 20 and 21 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 20 and 21 are drawn to nucleic acids that encode a copalyl diphosphate synthase enzyme (hereinafter referred to as CPS) or a fragment thereof, wherein the nucleic acid hybridizes to SEQ ID NO: 7 or the complement of SEQ ID NO: 7. Claim 21 further stipulates that the nucleic acid which hybridizes to SEQ ID NO: 7 or it's complement comprises SEQ ID NO: 7 or it's complement. The claims encompass a peptide encoded by SEQ ID NO: 7 which has CPS activity, as well as homologues of SEQ ID NO: 7 which encode a peptide with CPS activity. Further, due to the use of the term comprising, the claims also encompass the full length gene and cDNA comprising SEQ ID NO: 7 as well as homologues of such, which encode a copalyl diphosphate synthase. The specification has only provided the sequence of SEQ ID NO: 7, but has provided no evidence that SEQ ID NO: 7 encodes a copalyl diphosphate synthase. The teachings of the art and a sequence alignment for SEQ ID NO: 7 provide strong evidence that SEQ ID NO: 7 does not encode a peptide with copalyl diphosphate synthase activity.

Alignment studies with the An1 (CPS) gene in maize and SEQ ID NO: 7 suggest that SEQ ID NO: 7 is only a partial fragment of a putative full length cDNA. The 93.4% similarity

exists with the portion of the nucleic acid which encodes the extreme C terminal end of An1. The art, however, teaches that such a fragment of An1 would not be expected to have copalyl diphosphate synthase activity. Smith et al (Plant Physiol. 1998, pages 1411-1419) teaches an alignment of plant CPS's including An1 (see Figure 1), and teaches that truncation mutants revealed that once the enzyme was truncated up to a certain point on the N-terminus in pumpkin CmCPS1 and CmCPS2, that such enzymes lacked activity (see figure 1, inverted triangle and legend). If SEQ ID NO: 7 encodes a fragment of a functional CPS, it is no where near this N terminal point. Additionally, Sakamoto et al (Plant Physiol. Vol. 134, pages 1642-1653, 2004) teaches that in rice, a number of CPS-like sequences were found, including one which turned out to be a non functional pseudogene (see table 1, OsCPS3). Sakamoto teaches that other homologues might have different functions than those for OsCPS1 and An1 (see page 1644, col. 2, last sentence of first full para). Sakamoto also teaches of the frequent presence of small pieces of CPS-like sequences in the rice genome (see page 1652, col. 1, last sentence of para 2). Thus, it is not clear that a full length cDNA that comprises SEQ ID NO: 7 even exists, and if so, if it would encode a functional CPS or a pseudogene.

The genus of nucleic acids encompassed by the claims is limited to nucleic acids which encode a copalyl diphosphate synthase and either comprise or hybridize to SEQ ID NO: 7 or its complement. However, as evidenced above, SEQ ID NO: 7 does not appear to encode a peptide with CPS activity. Further, there is evidence to suggest that a full length gene or cDNA may not exist. The specification teaches SEQ ID NO: 7, but provides no evidence that it encodes a peptide with CPS activity. The description of SEQ ID NO: 7 is therefore not representative of the genus of nucleic acids encompassed by the claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NOS: 7, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and proteins with copalyl diphosphate synthase activity they encode, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25

USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

***Response to Arguments***

The rejection set forth above is newly applied to claims 20 and 21. It has not been maintained for claims 10, 24, and 25. The arguments in the appeal brief as they apply to claims 20 and 21 have been thoroughly reviewed but were not found persuasive. The genus of nucleic acids encompassed by the claims is limited to nucleic acids which encode a copalyl diphosphate synthase and either comprise or hybridize to SEQ ID NO: 7 or its complement. However, as evidenced above, SEQ ID NO: 7 does not appear to encode a peptide with CPS activity. Further, there is evidence to suggest that a full length gene or cDNA may not exist. The specification teaches SEQ ID NO: 7, but provides no evidence that it encodes a peptide with CPS activity. The description of SEQ ID NO: 7 is therefore not representative of the genus of nucleic acids which encode a copalyl diphosphate synthase as encompassed by the claims. Further, other than generally disclosing methods of site directed mutagenesis, making fusion peptides, etc, the specification provides no description or guidance as to how to alter or construct a sequence comprising or hybridizing to SEQ ID NO: 7 which encodes a copalyl diphosphate synthase enzyme. No teaching is provided on how to specifically manipulate SEQ ID NO: 7 to obtain a sequence which encodes a copalyl diphosphate synthase. Claim 20 recites hybridization conditions and is not limited to the sequence of SEQ ID NO: 7 or its complement. As such, each member of the claimed genus does not contain the same structural feature, as is asserted at page 25 of the appeal brief. For those members that do contain SEQ ID NO: 7 or its complement, SEQ ID NO: 7 does not appear to encode a peptide with CPS enzymatic activity. As such, no

structure-function correlation is present with regard to this structural feature (SEQ ID NO: 7) and the genus of nucleic acids with the functional activity encompassed by the claims.

***Claim Rejections - 35 USC § 102***

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Bensen (Bensen et al, The Plant Cell, vol. 7, pages 75-84, 1995) or in the alternative Genbank Accession number L37750 (sequence alignment provided).

The Tm of SEQ ID NO: 7 was calculated using www.promega.com/biomath/calc11.htm. It was calculated to be 79 degrees C. Adjusting for salt, the Tm was calculated to be 74 degrees C. Given such, under the conditions specified in claim 20, the sequence taught by Bensen (figure 6) the maize An1 sequence which encodes a copalyl diphosphate synthase, which is the nucleic acid sequence of Genbank accession number L37750 would hybridize to the complement of SEQ ID NO: 7. Additionally, the claim recites "nucleic acid molecule comprises a nucleic acid sequence that hybridizes...". L37750 represents a nucleic acid molecule that "comprises" a nucleic acid sequence that would hybridize to SEQ ID NO: 7 or its complement. In other words, only the nucleic acid sequence of the larger nucleic acid molecule need hybridize to SEQ ID NO: 7 or its complement. As can be seen from the sequence alignment for SEQ ID NO: 7 and L37750, large portions of SEQ ID NO: 7, close to 200 nucleotides, are perfect matches with the

accession number. Such large portions would hybridize to the complement of SEQ ID NO: 7 under the specified conditions. For example, the salt adjusted Tm for the fragment starting on or about nucleotide 70 of SEQ ID NO: 7 and extending to nucleotide 255 is 71 degrees C. Therefor, the teachings of Bensen and Accession number L37750 anticipate the claimed invention.

***Response to Arguments***

10. The response (appeal brief filed 11/5/2004) traverses the rejection on the grounds that no evidence is provided to support the proposition that Genbank Accession Number L37750 would specifically hybridize to SEQ ID NO: 7 or a complement thereof. Firstly, it should be noted that claim 20 does not recite the term specifically. However, even if it did, this term, given it's broadest reasonable interpretation, would simply mean that the claim was drawn to nucleic acids that hybridized to SEQ ID NO: 7 or its complement. Further it should be noted that the claim does not recite "a" complement. The claimed recitation "its complement" has been interpreted to be limited to the complement of SEQ ID NO: 7, of which there is only one. In other words, "the complement" of SEQ ID NO: 7 is the sequence that is exactly complementary over its full length to the full length of SEQ ID NO: 7. The arguments regarding evidence have been considered and addressed in the rejection set forth above.

11. Claims 10, 20, 21, 24, and 25 is rejected under 35 U.S.C. 102(b) as being anticipated by Sigma catalog products O1256 or in the alternative O4378.

Product O1256 is a 4 mer oligonucleotide of poly dT and product O4378 is a 4 mer oligonucleotide of poly dA. The claim has been given its broadest reasonable interpretation. The hybridization conditions set forth in the claim only apply to the first nucleic acid "wherein said first nucleic acid molecule comprises a nucleic acid sequence that hybridizes...". However, the claim is drawn to a first nucleic acid molecule or fragment thereof. The 4mer poly dA sequence of Sigma catalog anticipates the 4 mer poly dA fragments of SEQ: 6 (for example, see nucleotides 433-436). Additionally, the response (appeal brief filed 11/5/2004) traverses the rejection on the grounds that no evidence is provided to support the proposition that Genbank Accession Number L37750 would specifically hybridize to SEQ ID NO: 7 or a complement thereof. While the claim recites "its complement" which was interpreted as "the complement" of SEQ ID NO: 7, it appears that the response treats such as 'a' complement. While "the complement" of SEQ ID NO: 7 is the sequence that is exactly complementary over its full length to the full length of SEQ ID NO: 7, 'a' complement could be any complementary sequence to SEQ ID NO: 7. The 4 mer poly dT product represents "a" complement of a fragment (AAAA) of SEQ ID NO: 7. Therefore, the products of the Sigma catalog anticipate the claimed nucleic acids. The rejection of claims 10, 21, 24, and 25 is based on the response's interpretation of the claimed recitation "its complement" (which is present in claims 10, 21, 24, and 25) as "a complement". The term "a" complement has been broadly interpreted above. The 4 mer poly dT product also represents "a" complement of SEQ ID NO: 7.

### *Response to Arguments*

12. The response (appeal brief filed 11/5/2004) traverses the rejection on the grounds that no evidence is provided to support the proposition that the products of Sigma catalog would specifically hybridize to SEQ ID NO: 7 or a complement thereof. Firstly, it should be noted that claim 20 does not recite the term specifically. However, even if it did, this term, given its broadest reasonable interpretation, would simply mean that the claim was drawn to nucleic acids that hybridized to SEQ ID NO: 7 or a complement. Any arguments with regard to hybridization conditions or evidence have been addressed in the claim interpretation as set forth above, in section 11.

### *Conclusion*

13. No claims are allowable.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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